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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/965,766	09/28/2001	Helmut Meissner	1/1150	3427

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EXAMINER	
HUANG, EVELYN MEI	

ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 04/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/965,766	MEISSNER ET AL.	
	Examiner	Art Unit	
	Evelyn Huang	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) *13-18 and 36-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12, 19-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-40 are pending. Claims 13-18, 36-40 have been withdrawn as being drawn to the non-elected invention. Cancellation of the non-elected subject matter is recommended.

Claim Rejections - 35 USC § 103

2. The rejection for Claims under 35 U.S.C. 103(a) as being obvious over Banholzer I (5770738) or Banholzer II (5654314, which has the same parent as 5770738), which are the US equivalents of WO 92/16528 (PTO-1449)) and the corresponding obviousness type double patenting rejection is withdrawn for claims 4-6, 10-12, 22-24, 28-30, 34, 35 (wherein both phenyls are substituted by fluoro, chloro or bromo) in view of the Declaration showing an unexpectedly shorter duration of action of the instant compound (wherein both phenyls are substituted by fluoro) over the compound of Banholzer (wherein both phenyls are unsubstituted). The instant compound therefore would fit in the pharmacological profile necessary for a once-a-day drug, whereas the compounds of Banholzer having an extremely long duration of action would not be useful for a once-a-day mode of administration.

The rejection, however, is maintained for claims 1-3, 7-12, 19-21, 25-27, 31-33 for reasons of record. Applicant argues that the claims have been amended so that both phenyls are substituted, the unexpected results in the Declaration by Dr. Pieper would obviate the 103 rejection.

However, the Declaration is deemed ineffective in overcoming the obviousness rejection for these claims. Unexpected results has not been established because the comparison is not made with the closest inventive compound with the prior art compound with only one difference. In the Declaration, the comparison is made with the instant Example 34 and Example 35, which is fluoro-substituted on both phenyls, with Example 10 of of Banholzer I or II, which has an unsubstituted phenyl. The instant Example 34 or Example 35 is not the closest compound for comparison. The instant claims as recited encompass a compound with both phenyls substituted with methyl, which is much closer to the prior art compound (with unsubstituted phenyls) than the instant Example 34 or 35 (with fluoro-substituted phenyls).

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 19-24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The 'diseases that benefits from treatment with anticholinergics reaches out to diseases not yet identified at present.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 19-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making and using the inventive compound for treating asthma or COPD, spasm in the gastrointestinal tract or spasm in the urinary tract, does not reasonably provide enablement for the use of the inventive compound for treating all the diseases as recited. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

a. *Nature of the invention.*

The instant invention is drawn to a dehydrotropanyl or epoxytropanyl compound for use in treating a disease that benefits from treatment with anticholinergics in a patient, including the diseases as recited on pages 50-51 of the specification.

b. *State of the prior art and level of skill of the artisan.*

Different subtypes of muscarinc receptors are known to have different pharmacological effects on various target tissues (van Zwieten et al. Cardiovascular drugs and therapy/sponsored by the International Society of Cardiovascular Pharmacotherapy, 1995, 9(1) : 159-67, especially page 160, Table 1). Tropinyl esters with antimuscarinic activity has been described (Xu et al. Chemical & Pharmaceutical Bulletin, 1998, 46(2): 231-41). Anticholinergic dehydrotropanyl or epoxytropanyl-xanthene carboxylate compound similar to the instant is known (Banholzer I (5770738), Banholzer II (5654314)). M3 receptors are known to be involved in chronic obstructive airway disease, gastrointestinal or urinary tract spasms (Xu, page 231, first paragraph; van Zweieten, page 164, column 1). The nexus of anticholinergics and vagally induced sinus bradycardia, heart rhythm disorders, or menstrual pain as recited in the instant has not been established

The level of skill of the artisan in the anticholinergic art is high.

c. *Predictability/unpredictability of the art.*

The high degree of unpredictability in the anticholinergic art is well known. A slight change in the structure of the compound would drastically change its selectivity for the receptor and its inhibitory activity as evidenced in the very different pK_{EC50} values exhibited by the structurally very similar compounds (Xu, page 233, Table 1).

d. *Amount of guidance/working examples.*

The preparation of 7 example compounds has been described. An example of a pharmaceutical composition comprising multiple active ingredients has not been described.

The procedures for assessing the in vitro or in vivo biological activity of the inventive compound are not described.

e. *The breadth of the claims.*

Applicant's assertion that the inventive compounds would be useful for treating any disease that benefits from treatment with any subtypes of anticholinergics, (including diseases not yet identified), does not commensurate with the scope of the objective enablement, especially in view of the high degree of unpredictability in the art and the absence of working examples.

f. *Quantitation of undue experimentation.*

Since insufficient teaching and guidance have been provided in the specification (paragraph c-e above), one of ordinary skill in the art, even with high degree of skill, would not be able to use the compounds as claimed without undue experimentation except for making and using the invention compound for treating asthma, COPD, spasm in the gastrointestinal tract or spasm in the urinary tract.

Double Patenting

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-12, 19-35 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9, 11-24 of U.S. Patent No. 6706726 (Application No. 09/976950) in view of Banholzer (WO 92/16528, PTO-1449).

The patented compound has hydrogen, lower alkoxy, lower alkyl or $-CH_2OH$ whereas the instant has a hydroxy as R^7. However, in a similar anti-cholinergic compound, Banholzer teaches that hydroxy, hydrogen, lower alkoxy, lower alkyl or $-CH_2OH$ are all optional choices (page 2, definition of R_1). Examples for the various R_1 substituents are shown in Table II and Table V).

One of ordinary skill in the art would be motivated to replace the hydrogen, lower alkoxy, lower alkyl or $-CH_2OH$ of the patented compound with the alternative, exemplified hydroxy to arrive at the instant invention with the reasonable expectation to obtain an additional compound useful as an anti-cholinergic agent.

Conclusion

6. No claims are allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Evelyn Huang whose telephone number is 571-272-0686. The examiner can normally be reached on Tuesday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Evelyn Huang
Primary Examiner
Art Unit 1625